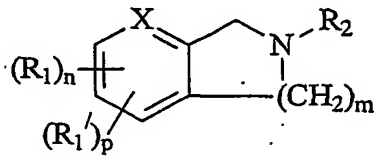
CLAIMS

1. Use of a compound of the formula (I), or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in the treatment or prevention of a condition involving sodium ion flux through a sensory neurone specific channel of a sensory neurone



(I)

wherein:

- X is -N- or -CH-;
- n is from 0 to 3;
- each R_1 is the same or different and is a hydroxy, amino, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyloxy, C_2-C_6 alkynyloxy, C_1-C_6 haloalkoxy, C_1-C_6 alkylthio, C_1-C_6 haloalkylthio, (C_1C_6 alkyl)amino or di(C_1-C_6 alkyl)amino group;
- p is 0 or 1;
- R_1' is cyano, -$NR_/$-CO-(C_1-C_4 alkyl), -$NR_/$-$S(O)_2$-(C_1-C_4 alkyl), -CO_2H, -$S(O)_2OH$, -CO_2-(C_1-C_4 alkyl), -O-$S(O)_2$-(C_1-C_4 alkyl) or -N[$S(O)_2$-(C_1-C_4 alkyl)]$_2$, wherein $R_/$ is hydrogen or a C_1-C_4 alkyl group;
- m is 1, 2 or 3; and
- R_2 is either

(a) -L-A, wherein L is a direct bond or a C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl moiety and A is C_6-C_{10} aryl, C_3-C_6 carbocyclyl, a 5- to 10- membered heteroaryl group or a 5- to 10- membered heterocyclic group,

(b) -L-$CR(A)_2$ or -L-$CH=C(A)_2$ wherein R is hydrogen or C_1-C_4 alkyl, L is as defined above and each A is the same or different and is as defined above,

(c) -L'-Het-A', wherein Het is -O-, -S- or -NR'-, A' is -L-A, -L-$CR(A)_2$ or -L-$CH=C(A)_2$, R' is H or -L-A, L' is a C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl moiety, L is as defined above, R is as defined above and each A is the same or different and is as defined above,

(d) -L-CO-NR_3R_4 or -L-CS-NR_3R_4, wherein L is as defined above and either (i) R_3 and R_4, together with the N atom to which they are attached, form a 5- to 10- membered heteroaryl or heterocyclyl group or (ii) R_3 represents -L-H or A′ wherein L and A′ are as defined above, and R_4 represents -L′-H, -L′-CO-A′, -L′-S(O)-A′, -L′-$S(O)_2$-A′, -L′-Het-A′, -NR-CO-$N(A)_2$, -$N(A)_2$, -A-Het-A, -A′, -L-$CR(LA)_2$ or -L-CH=$C(LA)_2$ wherein each L is the same or different, each A is the same or different, and L′, L, R, A and A′ are as defined above,

(e) -CO-L-NR_3R_4 or -CS-L-NR_3R_4 wherein L, R_3 and R_4 are as defined above,

(f) -CO-A′ or -CS-A′ wherein A′ is as defined above,

(g) -L′-O-N=$C(A)_2$ or -CO-L′-O-N=$C(A)_2$ wherein L′ is as defined above and each A is the same or different and is as defined above, or

(h) -L′-NR-CO-NR_3R_4 or -L′-NR-CS-NR_3R_4, wherein L′, R, R_3 and R_4 are as defined above,

wherein

- said aryl, carbocyclyl, heteroaryl and heterocyclyl groups are optionally fused to one or two cyclic moieties selected from phenyl rings and 5- to 6- membered heterocyclyl and heteroaryl groups, and
- said aryl, heteroaryl, carbocyclyl and heterocyclyl groups are unsubstituted or are substituted by 1, 2 or 3 substituents which are the same or different and are selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halogen, hydroxy, amino, (C_1-C_4 alkyl)amino, di(C_1-C_4 alkyl)amino, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 haloalkylthio, -NH-CO-(C_1-C_4 alkyl), -CO-(C_1-C_4 alkyl), -CO_2-(C_1-C_4 alkyl), 5- or 6- membered heteroaryl, phenyl and -$CHPh_2$ substituents, the phenyl and heteroaryl moieties in said substituents being unsubstituted or substituted by 1 or 2 further substituents selected from halogen atoms, C_1-C_2 alkyl groups, C_1-C_2 alkoxy groups and -NH-CO-(C_1-C_2 alkyl) groups,

provided that (a) when R_2 is -L-A, A is other than a benzimidazolyl group, and (b) when R_2 is -CO-A′ or -CS-A′, A is other than a pyrazolopyrimidinyl or pyrazolyl group.

2. Use according to claim 1, wherein:

- X is -N- or -CH-;

- n is from 0 to 3;
- p is 0;
- each R_1 is the same or different and is a hydroxy, amino, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_6 alkylthio, C_1-C_6 haloalkylthio, (C_1C_6 alkyl)amino or di(C_1-C_6 alkyl)amino group;
- m is 1, 2 or 3; and
- R_2 is either

(a) -L-A, wherein L is a direct bond or a C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl moiety and A is C_6-C_{10} aryl, C_3-C_6 carbocyclyl, a 5- to 10- membered heteroaryl group or a 5- to 10- membered heterocyclic group,

(b) -L-CR(A)$_2$ or -L-CH=C(A)$_2$ wherein R is hydrogen or C_1-C_4 alkyl, L is as defined above and each A is the same or different and is as defined above,

(c) -L′-Het-A′, wherein Het is -O-, -S- or -NR′-, A′ is -L-A, -L-CR(A)$_2$ or -L-CH=C(A)$_2$, R′ is H or -L-A, L′ is a C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl moiety, L is as defined above, R is as defined above and each A is the same or different and is as defined above,

(d) -L-CO-NR$_3$R$_4$ or -L-CS-NR$_3$R$_4$, wherein L is as defined above and either (i) R_3 and R_4, together with the N atom to which they are attached, form a 5- to 10- membered heteroaryl or heterocyclyl group or (ii) R_3 represents -L-H or A′ wherein L and A′ are as defined above, and R_4 represents -L′-H, -L′-CO-A, A′, -L-CR(LA)$_2$ or -L-CH=C(LA)$_2$ wherein each L is the same or different, each A is the same or different, and L′, L, R, A and A′ are as defined above,

(e) -CO-L-NR$_3$R$_4$ or -CS-L-NR$_3$R$_4$ wherein L, R_3 and R_4 are as defined above,

(f) -CO-A′ or –CS-A′ wherein A′ is as defined above, or

(g) -L′-O-N=C(A)$_2$ or -CO-L′-O-N=C(A)$_2$ wherein L′ is as defined above and each A is the same or different and is as defined above,

wherein

- said aryl, carbocyclyl, heteroaryl and heterocyclyl groups are optionally fused to one or two cyclic moieties selected from phenyl rings and 5- to 6- membered heterocyclyl and heteroaryl groups, and
- said aryl, heteroaryl, carbocyclyl and heterocyclyl groups are unsubstituted or are substituted by 1, 2 or 3 substituents which are the same or different and are selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halogen, hydroxy, C_1-C_4 alkoxy, C_1-C_4

haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 haloalkylthio, phenyl and -$CHPh_2$ substituents, the phenyl moieties in said substituents being unsubstituted or substituted by 1 or 2 halogen atoms,

provided that (a) when R_2 is -L-A, A is other than a benzimidazolyl group and (b) when R_2 is -CO-A′ or -CS-A′, A is other than a pyrazolopyrimidinyl or pyrazolyl group.

3. Use according to claim 1 or 2, wherein the aryl, heteroaryl, heterocyclyl and carbocyclyl groups and moieties in the substituents R_1, R_2, R_3 and R_4 are unsubstituted or substituted by 1, 2 or 3 substituents which are the same or different and are selected from halogen, C_1-C_4 alkyl, hydroxy, amino, (C_1-C_4 alkyl)amino, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 haloalkylthio, -NH-CO-(C_1-C_2 alkyl), -CO-(C_1-C_2 alkyl), -CO_2-(C_1-C_2 alkyl), 5- membered heteroaryl, phenyl and -$CHPh_2$ substituents, the phenyl and heteroaryl moieties in said substituents being unsubstituted or substituted by one or two further substituents selected from halogen atom, C_1-C_2 alkyl groups, C_1-C_2 alkoxy groups and -NH-CO-(C_1-C_2 alkyl) groups.

4. Use according to any one of the preceding claims, wherein each R_1 is the same or different and is a hydroxy, amino, halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio or C_1-C_4 haloalkylthio group.

5. Use according to any one of the preceding claims, wherein each L moiety in the R_2 substituent is the same or different and represents a direct bond or a C_1-C_4 alkyl moiety and/or each L′ moiety in the R_2 substituent is the same or different and represents a C_1-C_4 alkyl moiety.

6. Use according to any one of the preceding claims, wherein each A moiety in the R_2 substituent is the same or different and represents a C_6-C_{10} aryl, C_3-C_6 cycloalkyl, 5- or 6- membered heterocyclyl or 5- or 6- membered heteroaryl group, which group is (a) unsubstituted or substituted by 1, 2 or 3 substituents selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, halogen, hydroxy, amino, (C_1-C_4 alkyl)amino, di(C_1-C_4

alkyl)amino, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkylthio, C_1-C_4 haloalkylthio, -NH-CO-(C_1-C_2 alkyl), phenyl and halophenyl substituents and (b) optionally fused to one or two cyclic moieties selected from phenyl rings and 5- to 6- membered heterocyclyl or heteroaryl groups.

7. Use according to any one of the preceding claims, wherein each R substituent in each -$CR(A)_2$ moiety is the same or different and is hydrogen or methyl.

8. Use according to any one of the preceding claims, wherein each Het moiety in the R_2 substituent is -O-, -S- or -NR'- wherein R' is hydrogen, C_1-C_4 alkyl, phenyl or -(C_1-C_4 alkyl)-phenyl.

9. Use according to any one of the preceding claims, wherein, when R_3 and R_4, together with the nitrogen atom to which they are attached, form a heterocycle, they form a 5- to 7- membered heterocyclyl group.

10. Use according to claim 9, wherein, when R_3 and R_4, together with the nitrogen atom to which they are attached, form a heterocycle, they form a morpholino, thiomorpholino, S-oxo-thiomorpholino, S,S-dioxo-thiomorpholino, pyrrolidinyl, piperazinyl or homopiperidinyl ring which is (a) optionally fused to one or two cyclic moieties selected from phenyl rings and 5- to 6- membered heteroaryl rings, and (b) unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, halogen, phenyl, -$CHPh_2$, -CO-(C_1-C_2 alkyl), -CO_2-(C_1-C_2 alkyl) and 5- to 6- membered heteroaryl substituents, the phenyl and heteroaryl moieties in said substituents being unsubstituted or substituted by 1 or 2 further substituents selected from halogen atoms, C_1-C_2 alkyl groups, C_1-C_2 alkoxy groups and -NH-CO(C_1-C_2 alkyl) groups.

11. Use according to any one of the preceding claims, wherein, when R_3 and R_4 do not together form a heterocycle, R_3 represents hydrogen or a C_1-C_4 alkyl, phenyl, -(C_1-C_4 alkyl)-phenyl or -(C_1-C_4 alkyl)-$CHPh_2$ group in which the phenyl moieties are unsubstituted or substituted by a hydroxy group and R_4 represents C_1-C_4 alkyl, A, -(C_1-C_4 alkyl)-A, -$(CH_2)_m$-$CH(A)_2$, -$CH[(CH_2)_mA]_2$, -$(CH_2)_m$-CO-A, -$(CH_2)_m$-O-

$CH(A)_2$, $-(CH_2)_m-S-CH(A)_2$, $-(CH_2)_m-S(O)-CH(A)_2$, $-(CH_2)_m-S(O)_2-CH(A)_2$, -NH-CO-$N(A)_2$, $-N(A)_2$ or -A-O-A, wherein each A is the same or different and is as defined above and m is 0, 1, 2, 3 or 4, the A moieties in the R_4 substituent being (a) unsubstituted or substituted by one or two substituents selected from C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, hydroxy, amino, C_1-C_2 haloalkyl, C_1-C_2 haloalkoxy and C_1-C_2 haloalkylthio substituents and (b) monocyclic or fused to one or two phenyl rings.

12. Use according to any one of the preceding claims, wherein, when R_2 is defined according to option (a), A is monocyclic.

13. Use according to any one of the preceding claims, wherein, when R_2 is defined according to option (f), A is a said C_6-C_{10} aryl group.

14. Use according to any one of the preceding claims, wherein

- X is -N- or -CH-;
- n is 0 or 1;
- each R_1 is the same or different and is C_1-C_2 alkyl, hydroxy or C_1-C_2 alkoxy;
- p is 0 or 1;
- R_1' is cyano, $-NH-CO-CH_3$, $-NH-S(O)_2-CH_3$, $-O-S(O)_2-CH_3$, $-N[SO_2-CH_3]_2$ or $-S(O)_2-OH$;
- m is 1, 2 or 3; and
- R_2 is either

(a) -L-A wherein L represents a direct bond or a C_1-C_4 alkyl moiety, for example a methyl, ethyl or propyl moiety, and A is a phenyl, thienyl, triazolyl, pyridyl, fluorenyl, thiazolyl, tetrahydroisoquinolinyl, 9H-carbazolyl, indolinyl, 9H-xanthenyl or benzimidazolyl group, which group is unsubstituted or substituted by one or two substituents selected from halogen, C_1-C_2 alkyl, hydroxy, amino, C_1-C_2 alkoxy, C_1-C_2 haloalkyl, C_1-C_2 haloalkoxy, C_1-C_2 haloalkylthio, $-NH-CO-CH_3$ and phenyl substituents,

(b) $-L-CR(A)_2$ or $-L-CH=C(A)_2$ wherein R is hydrogen or methyl, L is as defined above and each A is the same or different and is as defined above,

(c) $-L'-Het-A'$ wherein Het is -O- or $-NR'-$ wherein R' is hydrogen, C_1-C_4 alkyl or benzyl, A' is -L-A, $-L-CR(A)_2$ or $-L-CH=C(A)_2$, L' is a C_1-C_4 alkyl moiety,

for example a methyl, ethyl or propyl moiety, L is as defined above, R is as defined above and each A is the same or different and is as defined above,

(d) -L-CO-NR_3R_4 wherein L is as defined above and either (i) R_3 and R_4, together with the nitrogen atom to which they are attached, form a morpholino, thiomorpholino, S-oxo-thiomorpholino, S,S-dioxo-thiomorpholino, pyrrolidinyl, piperazinyl or homopiperidinyl ring which is (a) optionally fused to one or two cyclic moieties selected from phenyl rings and 5- to 6-membered heteroaryl rings, and (b) unsubstituted or substituted by one or two substituents selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, halogen, phenyl, -$CHPh_2$, -CO-(C_1-C_2 alkyl), -CO_2-(C_1-C_2 alkyl) and 5- to 6-membered heteroaryl substituents, the phenyl and heteroaryl moieties in said substituents being unsubstituted or substituted by one or two further substituents selected from halogen atoms, C_1-C_2 alkyl groups, C_1-C_2 alkoxy groups and -NH-CO-(C_1-C_2 alkyl) groups, or (ii) R_3 represents hydrogen, C_1-C_4 alkyl or an unsubstituted benzyl, phenyl, hydroxyphenyl or -(C_1-C_2 alkyl)-$CHPh_2$ group and R_4 represents C_1-C_4 alkyl, fluorenyl, phenyl, pyridyl, -(C_1-C_4 alkyl)-phenyl, -(C_1-C_4 alkyl)-(5- to 6- membered heteroaryl), -$(CH_2)_m$-(9H-carbazolyl), -$(CH_2)_m$-indolinyl, -$(CH_2)_m$-(9H-xanthenyl), -$(CH_2)_m$-O-$CHA''A'''$, -$(CH_2)_m$-S-$CHA''A'''$, -$(CH_2)_m$-S(O)-$CHA''A'''$, -$(CH_2)_m$-$S(O)_2$-$CHA''A'''$, -NH-CO-$N(phenyl)_2$, -$N(phenyl)_2$ or -A''-O-A''', -$(CH_2)_m$-$CHA''A'''$, -$CH[(CH_2)_nPh]_2$ or -$(CH_2)_p$-CO-R where m is 0, 1, 2 or 3, A'' and A''' are the same or different and each represent phenyl or a 5- or 6-membered heteroaryl group, n is 0, 1 or 2, p is 1, 2 or 3 and R is 5- or 6-membered heterocyclic group fused to a phenyl ring, for example a tetrahydroisoquinoline group, the cyclic moieties in said R_4 groups being unsubstituted or substituted by a halogen atom, C_1-C_2 alkyl, hydroxy, amino or C_1-C_2 alkoxy group,

(e) -CO-L-NR_3R_4 or -CS-L-NR_3R_4 wherein L, R_3 and R_4 are as defined above,

(f) -CO-A′ or -CS-A′ where A′ is as defined above;

(g) -CO-L′-O-N=$C(A)_2$ wherein L′ is as defined above and each A is the same or different and is as defined above; or

(h) -L′-NR-CO-NR_3R_4 or -L′-NR-CS-NR_3R_4 wherein L′, R, R_3 and R_4 are as defined above,

provided that when R_2 is -L-A, A is monocyclic.

15. Use according to any one of the preceding claims, wherein said condition is chronic or acute pain, a bowel disorder, a bladder dysfunction, tinnitus or a demyelinating disease.

16. A compound of the formula (I), as defined in any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising a compound of the formula (I), as defined in any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

18. A composition according to claim 17 which is a capsule or tablet comprising from 10 to 500 mg of a compound of the formula (I), as defined in any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof.

19. An inhalation device comprising a pharmaceutical composition according to claim 18.

20. An inhalation device according to claim 19 which is a nebulizer.

21. A compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, for use in the treatment of the human or animal body.

22. A method of treating a patient suffering from or susceptible to a condition as defined in claim 1 or 15, which method comprises administering to said patient an effective amount of a compound of formula (I), as defined in any of claims 1 to 14, or a pharmaceutically acceptable salt thereof.